CLAIMS

What is claimed is:

1. A method of treating or preventing a myelodysplastic syndrome, which comprises administering to a patient in need of such treatment or prevention a therapeutically or prophylactically effective amount of a selective cytokine inhibitory drug, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof.

2. A method of managing a myelodysplastic syndrome, which comprises administering to a patient in need of such management a prophylactically effective amount of a selective cytokine inhibitory drug, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof.

3. A method of treating or preventing a myelodysplastic syndrome, which comprises administering to a patient in need of such treatment or prevention a therapeutically or prophylactically effective amount of a selective cytokine inhibitory drug, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof, and a therapeutically or prophylactically effective amount of at least one second active ingredient.

4. A method of managing a myelodysplastic syndrome, which comprises administering to a patient in need of such management a prophylactically effective amount of a selective cytokine inhibitory drug, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof, and a therapeutically or prophylactically effective amount of at least one second active ingredient.

5. The method of claim 3 or 4, wherein the second active ingredient is capable of improving blood cell production.

6. The method of claim 3 or 4, wherein the second active ingredient is a cytokine, hematopoietic growth factor, anti-cancer agent, antibiotic, proteasome inhibitor, or immunosuppressive agent.

7. The method of claim 3 or 4, wherein the second active ingredient is etanercept, imatinib, anti-TNF-α antibodies, infliximab, G-CSF, GM-CSF, EPO, topotecan, pentoxifylline, ciprofloxacin, irinotecan, vinblastine, dexamethasone, IL2, IL8, IL18, Ara-C, vinorelbine, isotretinoin, 13-cis-retinoic acid, or a pharmacologically active mutant or derivative thereof.

8. The method of any one of claims 1 to 4, wherein the myelodysplastic syndrome is refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, refractory anemia with excess blasts in transformation, or chronic myelomonocytic leukemia.

9. The method of any one of claims 1 to 4, wherein the myelodysplastic syndrome is primary or secondary.

10. The method of any one of claims 1 to 4, wherein the stereoisomer of the selective cytokine inhibitory drug is an enantiomer.

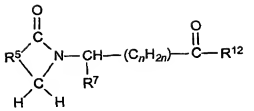
11. The method of any one of claims 1 to 4, wherein the selective cytokine inhibitory drug is 3-(3,4-dimethoxy-phenyl)-3-(1-oxo-1,3-dihydro-isoindol-2-yl)-propionamide.

12. The method of claim 11 wherein the selective cytokine inhibitory drug is the R or S enantiomer of 3-(3,4-dimethoxy-phenyl)-3-(1-oxo-1,3-dihydro-isoindol-2-yl)-propionamide.

13. The method of any one of claims 1 to 4, wherein the selective cytokine inhibitory drug is cyclopropanecarboxylic acid {2-[1-(3-ethoxy-4-methoxy-phenyl)-2-methanesulfonyl-ethyl]-3-oxo-2,3-dihydro-1 *H*-isoindol-4-yl}-amide.

14. The method of claim 13, wherein the selective cytokine inhibitory drug is the R or S enantiomer of cyclopropanecarboxylic acid {2-[1-(3-ethoxy-4-methoxy-phenyl)-2-methanesulfonyl-ethyl]-3-oxo-2,3-dihydro-1 *H*-isoindol-4-yl}-amide.

15. The method of any one of claims 1 to 4, wherein the selective cytokine inhibitory drug has formula (I):



(I)

wherein n has a value of 1, 2, or 3;

R^5 is o-phenylene, unsubstituted or substituted with 1 to 3 substituents each selected independently from the group consisting of nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, alkylamino, dialkylamino, acylamino, alkyl of 1 to 10 carbon atoms, alkyl of 1 to 10 carbon atoms, and halo;

R^7 is (i) phenyl or phenyl substituted with one or more substituents each selected independently of the other from the group consisting of nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, alkyl of 1 to 10 carbon atoms, alkoxy of 1 to 10 carbon atoms, and halo, (ii) benzyl unsubstituted or substituted with 1 to 3 substituents selected from the group consisting of nitro, cyano, trifluoromethyl, carbothoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, alkyl of 1 to 10 carbon atoms, alkoxy of 1 to 10 carbon atoms, and halo, (iii) naphthyl, and (iv) benzyloxy;

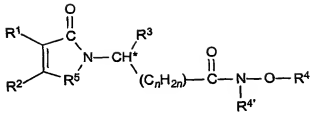
R^{12} is -OH, alkoxy of 1 to 12 carbon atoms, or

R^8 is hydrogen or alkyl of 1 to 10 carbon atoms; and

R^9 is hydrogen, alkyl of 1 to 10 carbon atoms, $-COR^{10}$, or $-SO_2R^{10}$, wherein R^{10} is hydrogen, alkyl of 1 to 10 carbon atoms, or phenyl.

16. The method of claim 15, wherein the selective cytokine inhibitory drug is enantiomerically pure.

17. The method of any one of claims 1 to 4, wherein the selective cytokine inhibitory drug has formula (II):



(II)

wherein each of R^1 and R^2, when taken independently of each other, is hydrogen, lower alkyl, or R^1 and R^2, when taken together with the depicted carbon atoms to which each is bound, is *o*-phenylene, *o*-naphthylene, or cyclohexene-1,2-diyl, unsubstituted or substituted with 1 to 3 substituents each selected independently from the group consisting of nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, alkylamino, dialkylamino, acylamino, alkyl of 1 to 10 carbon atoms, alkoxy of 1 to 10 carbon atoms, and halo;

R^3 is phenyl substituted with from one to four substituents selected from the group consisting of nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, alkyl of 1 to 10 carbon atoms, alkoxy of 1 to 10 carbon atoms, alkylthio of 1 to 10 carbon atoms, benzyloxy, cycloalkoxy of 3 to 6 carbon atoms, C_4-C_6-cycloalkylidenemethyl, C_3-C_{10}-alkylidenemethyl, indanyloxy, and halo;

R^4 is hydrogen, alkyl of 1 to 6 carbon atoms, phenyl, or benzyl;

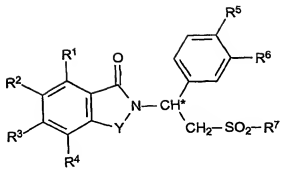
$R^{4'}$ is hydrogen or alkyl of 1 to 6 carbon atoms;

R^5 is $-CH_2-$, $-CH_2-CO-$, $-SO_2-$, -S-, or -NHCO-; and

n has a value of 0, 1, or 2.

18. The method of claim 17, wherein the selective cytokine inhibitory drug is enantiomerically pure.

19. The method of any one of claims 1 to 4, wherein the selective cytokine inhibitory drug has formula (III):



(III)

wherein the carbon atom designated * constitutes a center of chirality;

Y is C=O, CH2, SO_2, or $CH_2C=O$;

each of R^1, R^2, R^3, and R^4, independently of the others, is hydrogen, halo, alkyl of 1 to 3 carbon atoms, alkoxy of 1 to 3 carbon atoms, nitro, cyano, hydroxy, or $-NR^8R^9$; or any two of R^1, R^2, R^3, and R^4 on adjacent carbon atoms, together with the depicted phenylene ring are naphthylidene;

each of R^5 and R^6, independently of the other, is hydrogen, alkyl of 1 to 3 carbon atoms, alkoxy of 1 to 3 carbon atoms, cyano, or cycloalkoxy of up to 18 carbon atoms;

R^7 is hydroxy, alkyl of 1 to 8 carbon atoms, phenyl, benzyl, or $NR^{8'}R^{9'}$;

each of R^8 and R^9 taken independently of the other is hydrogen, alkyl of 1 to 8 carbon atoms, phenyl, or benzyl, or one of R^8 and R^9 is hydrogen and the other is $-COR^{10}$ or $-SO_2R^{10}$, or R^8 and R^9 taken together are tetramethylene, pentamethylene, hexamethylene, or $-CH_2CH_2X^1CH_2CH_2-$ in which X^1 is -O-, -S- or -NH-; and

each of $R^{8'}$ and $R^{9'}$ taken independently of the other is hydrogen, alkyl of 1 to 8 carbon atoms, phenyl, or benzyl, or one of $R^{8'}$ and $R^{9'}$ is hydrogen and the other is $-COR^{10'}$ or $-SO_2R^{10'}$, or $R^{8'}$ and $R^{9'}$ taken together are tetramethylene, pentamethylene, hexamethylene, or $-CH_2CH_2X^2CH_2CH_2-$ in which X^2 is -O-, -S-, or -NH-.

20. The method of claim 19, wherein the selective cytokine inhibitory drug is enantiomerically pure.

21. A method of treating, preventing or managing a myelodysplastic syndrome, which comprises administering to a patient in need of such treatment, prevention or management a therapeutically or prophylactically effective amount of a selective cytokine inhibitory drug, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof, before, during or after transplanting umbilical cord blood,

placental blood, peripheral blood stem cell, hematopoietic stem cell preparation or bone marrow into the patient.

22. A method of reducing or avoiding an adverse effect associated with the administration of a second active ingredient in a patient suffering from a myelodysplastic syndrome, which comprises administering to a patient in need of such reduction or avoidance an amount of the second active ingredient and a therapeutically or prophylactically effective amount of a selective cytokine inhibitory drug, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof.

23. The method of claim 22, wherein the second active ingredient is capable of improving blood cell production.

24. The method of claim 22, wherein the second active ingredient is a cytokine, hematopoietic growth factor, anti-cancer agent, antibiotic, proteasome inhibitor, or immunosuppressive agent.

25. The method of claim 22, wherein the second active ingredient is etanercept, imatinib, anti-TNF-α antibodies, infliximab, G-CSF, GM-CSF, EPO, topotecan, pentoxifylline, ciprofloxacin, irinotecan, vinblastine, dexamethasone, IL2, IL8, IL18, Ara-C, vinorelbine, isotretinoin, 13-cis-retinoic acid, or a pharmacologically active mutant or derivative thereof, or a combination thereof.

26. A pharmaceutical composition comprising a selective cytokine inhibitory drug, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof in an amount effective to treat, prevent or manage a myelodysplastic syndrome, and a carrier.

27. A pharmaceutical composition comprising a selective cytokine inhibitory drug, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof, and a second active ingredient.

28. The pharmaceutical composition of claim 27, wherein the second active ingredient is capable of improving blood cell production.

29. The pharmaceutical composition of claim 27, wherein the second active ingredient is a cytokine, hematopoietic growth factor, anti-cancer agent, antibiotic, proteasome inhibitor, or immunosuppressive agent.

30. The pharmaceutical composition of claim 27, wherein the second active ingredient is etanercept, imatinib, anti-TNF-α antibodies, infliximab, G-CSF, GM-CSF, EPO, topotecan, pentoxifylline, ciprofloxacin, irinotecan, vinblastine, dexamethasone, IL2, IL8, IL18, Ara-C, vinorelbine, isotretinoin, 13-cis-retinoic acid, or a pharmacologically active mutant or derivative thereof, or a combination thereof.

31. A single unit dosage form comprising a selective cytokine inhibitory drug, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof, and a second active ingredient capable of improving blood cell production.

32. A single unit dosage form comprising a selective cytokine inhibitory drug, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof, and a second active ingredient, wherein the second active ingredient is a cytokine, hematopoietic growth factor, anti-cancer agent, antibiotic, proteasome inhibitor, or immunosuppressive agent.

33. A single unit dosage form comprising a selective cytokine inhibitory drug, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof, and a second active ingredient selected from the group consisting of etanercept, imatinib, anti-TNF-α antibodies, infliximab, G-CSF, GM-CSF, EPO, topotecan, pentoxifylline, ciprofloxacin, irinotecan, vinblastine, dexamethasone, IL2, IL8, IL18, Ara-C, vinorelbine, isotretinoin, 13-cis-retinoic acid, or a pharmacologically active mutant or derivative thereof, and a combination thereof.

34. The single unit dosage form of claim 31, 32 or 33, wherein the dosage form is suitable for intravenous or subcutaneous administration to a patient.

35. A kit comprising:

a pharmaceutical composition comprising a selective cytokine inhibitory drug, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof; and

a pharmaceutical composition comprising a second active ingredient capable of improving blood cell production.

36. A kit comprising:

a pharmaceutical composition comprising a selective cytokine inhibitory drug, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof; and

umbilical cord blood, placental blood, peripheral blood stem cell, hematopoietic stem cell preparation or bone marrow.

37. The kit of claim 35 or 36 which further comprises a device for the administration of the pharmaceutical composition or the single unit dosage form.